Brief Communication

Sertoli cell only syndrome: Status of sertoli cell maturation and function

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ABSTRACT

Background of the study: Mature and functional Sertoli cells are essential for the survival of germ cells in testes. In Sertoli cell only syndrome (SCOS), there is no germ cells. Then, question arises whether absence of germ cells in SCOS secondary to Sertoli cells immaturity or mal function. Sertoli cells maturational and functional status is unclear in SCOS. This study investigated status of maturation and function of Sertoli cells in patients with SCOS. **Materials and Methods:** The present study was comprised of 37 cases of SCOS and 50 normal control males. Detailed clinical examination and investigation were carried out as per pre-determined proforma. Semen analysis, hormonal analysis (FSH, LH, testosterone, etc.), and fine needle aspiration cytology (FNAC) of testes (bilateral) were performed. Fluorescence *in situ* hybridization (FISH) with XY probes was carried out in addition to conventional chromosome analysis to find out chromosomal abnormalities, in particular sex chromosome aneuploidy, including mosaicism. Yq microdeletion status was also investigated. The anti-mullerian hormone (AMH), inhibin B, and seminal lactate were estimated by ELISA methods. **Results:** The study did not find any case of high AMH. About 78% cases had low inhibin B, and 60% had low AMH. FSH was high in about 78% cases. Low level of lactate was found in 49% cases. There was one case of high level of inhibin B. There were 6 (16.2%) cases of chromosomal abnormality (2 mosaic Klinefelter and 4 Klinefelter syndrome) and 4 (10.8%) cases of Yq microdeletion. **Conclusion:** We conclude that Sertoli cell immaturity does not play any role in SCOS (no case of high AMH). It seems, in majority cases, Sertoli cells are functionally- and/or numerically-deficient (low inhibin B, AMH and lactate). However, in about 22% cases, Sertoli cell function and/or number remains normal (normal inhibin B, AMH). Inhibin B and FSH seems best predictor/marker of Sertoli cell function.

Key words: Sertoli cell only syndrome, sertoli cells, anti-mullerian hormone, headings not required

SCOS applies to a testis, in which germ cells at any stage are absent, but the tubular architecture is not affected by fibrosis, and supporting cells continue to be present. Sertoli cells play a central role in development of a functional testis, and hence in the expression of a male phenotype. The Sertoli cells ensure regression of the Mullerian ducts via secretion of AMH. In the male, secretion of AMH by the Sertoli cells commences during embryogenesis and continues throughout life. AMH blood concentration decreases dramatically during puberty[1] and persists at low levels in adults.[2] Sertoli cells also produce inhibin B.[3] Sertoli cells produce lactate at a high rate.[4] To ensure germ cell survival, Sertoli cell must ensure lactate production, even in adverse conditions. Hence, it is important to recognize that absence of germ cells may also be a reflection of underlying abnormalities in the Sertoli cells, such as failure of their maturation. In order to assess the Sertoli cells maturation status and function, it is important to examine the markers such as inhibin B, AMH, and lactate.

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Infertile men with idiopathic SCOS were enrolled into the study. Study group comprised of 37 cases of SCOS. Medical history and details of clinical data were collected from the patients. About 5 ml EDTA blood were collected for DNA isolation/interphase FISH and 5 ml for serum

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to estimate inhibin B, AMH, FSH, lactate besides 1 ml of heparinized blood for cytogenetics. Fifty known fertile subjects were taken as control. An informed consent was obtained from each subject including controls.

Among 37 cases of SCOS, there were 6 cases of chromosomal abnormality (4 cases of Klinefelter syndrome and 2 cases of mosaic Klinefelter syndrome) and 4 cases of Yq microdeletions (2 cases of AZFbc and 1 each of AZFa and AZFc). We have found low level of AMH in 22 cases (59.45%). There was no case with high level of AMH. Similarly, we have found low level of inhibin B and high level of FSH in 29 cases (78.37%). There was one case of high level of inhibin B. Low seminal lactate was noted in 22 cases (59.45%). Table below is showing details of AMH, Inhibin B, Lactate, and FSH in control and SCOS cases.

Parameter	Control	SCOS Cases	*P* value
FSH (mIU/ml)	5.7 ± 2.9 (0.4/2.8 – 8.6)	26.1 ± 18.2 (2.2/7.9 – 44.3)	0.00001
Inhibin B (pg/ml)	165.6 ± 80.6 (11.4/85 – 246.2)	55.9 ± 64.7 (7.8/-8.7 – 120.6)	0.00001
AMH (ng/ml)	12.5 ± 6.3 (0.9/6.2 – 18.8)	4.7 ± 4.9 (0.6/-0.1 – 9.6)	0.00001
Lactate (nmol/μl)	61.6 ± 27.5 (3.9/34.2 – 89.1)	36 ± 25.2 (3/10.8 – 61.3)	0.00001

Value are given as mean + SD (SEM/range)

In this study, we have found a detectable cause in 27% (10/37) of cases (16.2% sex chromosomal abnormality and 10.8% Yq microdeletion), and remaining cases were idiopathic. We have also tried to find out Sertoli cell status through its biomarker AMH. We have found AMH either undetectable (mostly) or normal and no case with high level (expected in Sertoli cell immaturity or hyperplasia or tumor). This suggests that Sertoli cell immaturity or hyperplasia does not exist with SCOS. We hypothesize that Sertoli cells are either dysfunctional or scant in number in most SCOS. We have found inhibin B and FSH equally good predictor/marker of SCOS. We did not find any advantage of adding AMH as another marker over FSH and inhibin B and recommend FSH and inhibin B combination should be used to assess SCOS cases. Seminal lactate as a marker seems complex, and no co-relation was detectable (low, normal as well as high level seen). Furthermore, we did not find any differences in AMH, Inhibin B, and seminal lactate with or without chromosome abnormality or Yq microdeletion.

We concluded that there is an urgent need for more study in SCOS at genomic, epigenomic, and proteomic level to find out underlying etiology. This study should excite more specific work to explore underlying pathophysiology that, in future, could help in management of SCOS cases.

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